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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,583	PLESTED ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20-28 and 42-47* is/are pending in the application.

4a) Of the above claim(s) *24,25 and 42-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,20-23 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 05/10/04 in response to the non-final Office Action mailed 01/08/04. With this, Applicants have amended the specification.

Claims, as amended currently, are objected to because the lines are crowded too closely together making reading of lines difficult. In future, claims with double-spaced lines must be submitted.

Status of Claims

2) Claims 1-18 and 20-28 have been amended via the amendment filed 05/10/04.

Claims 19 and 29-41 have been canceled via the amendment filed 05/10/04.

New claims 42-47 have been added via the amendment filed 05/10/04. These claims are not drawn to elected subject matter, but to a mutant bacterium, classified in class 424, subclass 93.4. Accordingly, new claims 42-47 have been withdrawn from consideration. Because claims 24 and 25, as amended, are not directed any more to the elected product, these claims are withdrawn from consideration. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-18, 20-28 and 42-47 are pending.

Claims 1-18, 20-23 and 26-28 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 5(i) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the specification.

6) The objection to the specification made in paragraph 5(ii) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the specification.

7) The objection to the specification made in paragraph 5(iii) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the specification.

8) The objection to the specification made in paragraph 5(iv) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the specification.

9) The objection to the specification made in paragraph 5(v) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the specification.

10) The objection to claim 1 made in paragraph 15(a) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the claim.

11) The objection to claim 9 made in paragraph 15(b) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the claim.

12) The objection to claim 13 made in paragraph 15(c) of the Office Action mailed 01/08/04 is withdrawn.

13) The objection to claim 16 made in paragraph 15(d) of the Office Action mailed 01/08/04 is withdrawn in light of Applicants' amendment to the claim.

Objection(s) Maintained

14) The objection to the specification made in paragraph 5(iv) of the Office Action mailed 01/08/04 is maintained for reasons set forth therein and herebelow.

Applicants state that they have submitted an amended Figure 1 to address the objection. However, the amended Figure 1 submitted 05/10/04 does not depict any part of the structure in 'bold'. The objection stands.

Rejection(s) Moot

15) The rejection of claims 24 and 25 made in paragraph 7 of the Office Action mailed 0/08/04 under 35 U.S.C. § 112, first paragraph, is with regard to the deposit issue, is moot in light of Applicants' amendment to the claims that shifts the claims away from the elected invention.

16) The rejection of claims 24 and 25 made in paragraph 9(m) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' amendment to the claims that shifts away from the elected invention.

17) The rejection of claims 24 and 25 made in paragraph 9(q) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of

Applicants' amendment to the claims that shifts away from the elected invention.

18) The rejection of claim 24 made in paragraph 9(v) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' amendment to the claim that shifts away from the elected invention.

19) The rejection of claims 24 and 25 made in paragraph 9(x) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' amendment to the claim that shifts away from the elected invention.

20) The rejection of claims 24 and 25 made in paragraph 11 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Arumugham *et al.* (EP 0941738) as evidenced by Carbonetti *et al.* (US 5,736,361), is moot in light of Applicants' amendment to the claims that shifts away from the elected invention.

21) The rejection of claims 24 and 25 made in paragraph 13 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Plested *et al.* (*Infect. Immun.* 67: 5417-5426, October 1999 - Applicants' IDS), is moot in light of Applicants' amendment to the claims that shifts away from the elected invention.

Rejection(s) Withdrawn

22) The rejection of claim 16 made in paragraph 6 of the Office Action mailed 0/08/04 under 35 U.S.C. § 112, first paragraph, with regard to the deposit issue, is withdrawn in light of Applicants' amendment to the claim.

23) The rejection of claims 1-18, 20-23 and 26-28 made in paragraph 7 of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn.

24) The rejection of claim 1 made in paragraph 9(a) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

25) The rejection of claim 15 made in paragraph 9(b) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

26) The rejection of claims 1-3, 15, 17 and 18 made in paragraph 9(c) of the Office Action mailed

01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

27) The rejection of claims 15 and 17 made in paragraph 9(d) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

28) The rejection of claim 4 made in paragraph 9(e) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn.

29) The rejection of claims 6-8, 17 and 18 made in paragraph 9(f) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

30) The rejection of claims 9 and 10 made in paragraph 9(g) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

31) The rejection of claim 9 made in paragraph 9(h) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

32) The rejection of claim 27 made in paragraph 9(i) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

33) The rejection of claim 14 made in paragraph 9(j) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

34) The rejection of claim 9 made in paragraph 9(k) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

35) The rejection of claims 2, 3, 17 and 18 made in paragraph 9(l) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

36) The rejection of claims 2-18, 21-23 and 26-28 made in paragraph 9(m) of the Office Action

mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

37) The rejection of claim 21 made in paragraph 9(n) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

38) The rejection of claim 21 made in paragraph 9(o) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

39) The rejection of claims 22 and 23 made in paragraph 9(p) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

40) The rejection of claim 21 made in paragraph 9(r) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

41) The rejection of claim 21 made in paragraph 9(s) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

42) The rejection of claims 1 and 15 made in paragraph 9(t) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

43) The rejection of claim 14 made in paragraph 9(u) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

44) The rejection of claims 2-3, 6-8, 17 and 18 made in paragraph 9(w) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

45) The rejection of claims 2-18, 20-23 and 26-28 made in paragraph 9(x) of the Office Action mailed 01/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

46) The rejection of claims 1-12, 14-18, 20-23 and 26 made in paragraph 11 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Arumugham *et al.* (EP 0941738) as evidenced by Carbonetti *et al.* (US 5,736,361), is withdrawn in light of Applicants' amendments to the claims and/or the base clam(s).

47) The rejection of claims 1, 27 and 28 made in paragraph 12 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Kim *et al.* (*Infect. Immun.* 56: 2631-2638, 1988, already of record), is withdrawn in light of Applicants' amendment to the base claim(s). maintained for reasons set forth therein and herebelow.

Rejection(s) Maintained

48) The rejection of claim 14 made in paragraph 6 of the Office Action mailed 0/08/04 under 35 U.S.C. § 112, first paragraph, with regard to the deposit issue, is maintained for reasons set forth therein and herebelow.

Applicants contend that they have submitted a signed depository receipt for the hybridoma producing the B5 monoclonal antibody. Applicants state that the deposited cell line is the same as the one described in the specification.

Applicants' arguments have been carefully considered, but are non-persuasive. Submission of a signed depository receipt alone is not sufficient to overcome the rejection. As set forth in paragraph 6 of the Office Action mailed 0/08/04, a statement by an attorney of record who has the authority and control over the conditions of deposit stating that **all** restrictions upon public access to the deposit will be **irrevocably** removed upon the grant of a patent on this application, is required.

49) The rejection of claims 1-18 and 20-23 made in paragraph 13 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Plested *et al.* (*Infect. Immun.* 67: 5417-5426, October 1999 - Applicants' IDS), is maintained for reasons set forth therein and herebelow.

Applicants assert that the subject application claims priority from the US provisional application 60/156,940, filed 09/30/99, which precedes the October 1999 publication date of Plested. Applicants submit that Plested *et al.* is not an appropriate 35 U.S.C § 102(b) reference.

Applicants' arguments have been carefully considered, but are non-persuasive. Instant claims do not have full support and/or enabling disclosure in the provisional application, 60/156,940, filed 09/30/99. The vaccine as claimed that is capable of eliciting protective and/or immunoprophylactic

antibodies against the recited pathogenic *Neisseria* strain is not enabled or described in the provisional application. Plested *et al.* is properly applied under 35 U.S.C § 102(b) since instant claims are not granted priority to 09/30/99 because of the new matter contained in the claims, as amended. See below for the new matter that is identified in the claims.

50) The rejection of claims 1-12, 14-18, 20-22 and 26 made in paragraph 14 of the Office Action mailed 01/08/04 under 35 U.S.C § 102(b) as being anticipated by Verheul *et al.* (*Infect. Immun.* 59: 843-851, 1991, already of record) as evidenced by Plested *et al.* (*Infect. Immun.* 67: 5417-5426, October 1999 - Applicants' IDS), is maintained for reasons set forth therein and herebelow.

Applicants contend that what is claimed is an immunogenic component that 'consists of an epitope' on the *Neisseria* LPS inner core characterized by the presence of a PEtn moiety linked to position 3, 6, 7 or a combination thereof of HepII of the inner core LPS. Applicants assert that Verheul *et al.* do not demonstrate that the PEtn moiety of LPS is immunogenic. Applicants state that Verheul *et al.* demonstrate antibody responses directed against phosphate containing epitopes. Applicants allege that Verheul *et al.* do not demonstrate that the PEtn moiety of the inner core LPS is an exposed epitope and that Verheul's LPS conjugates comprise outer core LPS, which would be expected to mask reactivity to epitopes in the inner core LPS. Applicants submit that one skilled in the art would not accept Verheul as a credible reference teaching that PEtn is the epitope recognized by the antibodies. Applicants argue that Verheul *et al.* did not demonstrate that the elicited antibodies are opsonic, bactericidal, or in any way protective. Applicants conclude that based on Verheul *et al.*, it is not credible that a vaccine comprising a phosphoethanolamine moiety linked to position 3, 6, 7 or a combination thereof of HepII of the inner core is useful for the treatment of disease caused by pathogenic *Neisseria*.

Applicants' arguments have been carefully considered, but are non-persuasive. Applicants' arguments are not commensurate in scope with what is claimed in the instant claims. Contrary to Applicants' assertion, what is claimed is a vaccine '*comprising at least* one immunogenic component, said immunogenic component being an epitope on a *Neisseria* lipopolysaccharide inner core *characterized by* the presence of a phosphoethanolamine moiety linked to position 3, 6, 7, or a combination thereof, of HepII of the inner core'. Applicants are reminded that the transitional limitations "having", "comprising", "including," "containing," or "characterized by," represent open-

ended claim language and therefore, do not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Therefore, the limitation "comprising" or "characterized by" in the instant claim(s) allows additional elements or moieties, such as, an LPS outer core, to be present in the recited 'immunogenic component'. It should be noted that the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. *In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ("consisting of" defined as "closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith."). Furthermore, the limitation 'at least one immunogenic component' permits the presence of elements other than the recited LPS inner core, such as, outer core, to be present in the claimed vaccine. In other words, an LPS outer core is not excluded from the scope of the recited immunogenic component or the vaccine claimed in the instant claims. Additionally, since the 'at least one immunogenic component' is not recited to be isolated or purified, it reads on LPS inner core-containing whole cells, cell lysates and whole LPS with or without some or all of outer core.

Contrary to Applicants' arguments, the instant claims do not claim a vaccine comprising an immunogenic component 'consisting of an epitope' of the *Neisseria* LPS inner core. Instant claims do not use the closed claim language 'consists of'. Verheul *et al.* do not have to demonstrate that the PEtn moiety is immunogenic, or the PEtn moiety of the inner core LPS is an exposed epitope, since instant claims do not include such limitations. With regard to Applicants' argument that one skilled in the art would not accept Verheul as a credible reference, it should be noted that those skilled in the art, for example Plested *et al.* (*Infect. Immun.* 67: 5417-5426, October 1999 - Applicants' IDS), have accepted that some antibodies elicited by Verheul's oligosaccharide conjugate vaccine, comprising PEtn in the 3-position of HepII, have immunogenic and opsonophagocytic, i.e., protective and/or immunoprophylactic, activity (see paragraph bridging pages 5424 and 5425). Claim 1 does not require 'the PEtn moiety' to be immunogenic or to elicit protective and/or immunoprophylactic antibodies. As long as the claimed 'vaccine' comprises 'at

least one immunogenic component' that includes a PEtn-containing HepII moiety and has the 'capability' to elicit protective and/or immunoprophylactic antibodies against a pathogenic *Neisseria*, such a vaccine anticipates the claim. Verheul *et al.* taught just that.

As set forth at paragraph 14 of the Office Action mailed 01/08/04, Verheul *et al.* taught meningococcal L2 and meningococcal L3, L7,9 phosphoethanolamine-containing oligosaccharide-protein conjugates that are immunogenic in rabbits, with or without the use of Quil A adjuvant, and that elicit high levels of IgG antibodies specific to PEA-containing epitopes. Rabbits were also immunized with the unconjugated LPS (see page 845, left column, first full paragraph). LPS alone and LPS conjugates elicited specific IgG responses (see Figure 3 and page 848). Verheul *et al.* also taught whole cell meningococcal bacteria which elicit antibodies directed against PEA-containing epitopes (see abstract; and page 850, left column). The structure of the meningococcal LOS is depicted in Figure 1 which shows the presence of heptoses, KDO, GluNAc, glucose and PEA. By ELISA and inhibition ELISA, the conjugate-induced antibodies were shown to be reactive with PEA-containing whole meningococcal organisms (and therefore with accessible epitopes), LOS and OS (see page 850). That the antibodies elicited by the prior art vaccine are specific to PEtn in the 3-position of HepII and are opsonophagocytically functional, i.e., protective and/or immunoprophylactic, is inherent from the teachings of Verheul *et al.* in light of what is known in the art. For instance, Plested *et al.* taught that some antibodies elicited by Verheul's oligosaccharide conjugate vaccine comprising PEtn in the 3-position of HepII have immunogenic and opsonophagocytic, i.e., protective and/or immunoprophylactic, activity (see paragraph bridging pages 5424 and 5425). Because of the presence of the PEtn in the 3-position of HepII in the prior art composition, it is expected to react with the monoclonal antibody produced by the hybridoma deposited under the accession number IDAC 260900-1. Since the prior art inner core LPS contains the phosphoethanolamine-containing epitope similar to the one recited, the prior art product is expected to elicit functional antibodies to at least 60% to 95% of the strains within *N. meningitidis*.

In this regard, it is very important to note that the instant specification itself acknowledges that Verheul's composition comprising PEtn in the 3-position of Hep-II is immunogenic and elicits opsonophagocytosis. For example, the paragraph bridging pages 34 and 35 of the instant specification states as follows:

> Previous studies with oligosaccharide conjugates in mice and rabbits have demonstrated that PEtn is important in immunogenicity and functional activity of polyclonal antibodies (Verheul, A.F., *et al.*, 1991. Infect Immtm 59: 843-851). These studies identified two sets of polyclonal antibodies. One set resulting from L1 and 1-3,7,9 oligosaccharides had **PEtn in the 3-position of HepII**, were immunogenic, had **opsonophagocytic (OP)** and chemiluminescence in oxidative burst reactions but had no serum bactericidal activity. [Emphasis added].

The rejection stands.

New Rejection(s)

Applicants are asked to note the new rejection(s) made in this Office Action. Applicants' amendments necessitated the new ground(s) of rejection presented in this Office Action.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

51) Claims 9 and 10 are rejected under 35 U.S.C § 112, first paragraph, as being as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The newly added limitation, 'structural' equivalent thereof, in claims 9 and 10 is new matter, because there is no descriptive support for the limitation in the instant specification. Therefore, the limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or to point to specific pages and line numbers in the originally filed specification where support for such a recitation can be found.

52) Claim 20 is rejected under 35 U.S.C § 112, first paragraph, as being as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 20, as amended, includes the limitation, 'a lipopolysaccharide outer core of a bacterial capsule'. However, there is no descriptive support for the limitation in the instant specification, as originally filed. Therefore, the limitation in the claims is considered to be new matter. *In re*

Rasmussen, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim, or to point to specific pages and line numbers in the originally filed specification where support for the above-identified recitation can be found.

53) Claims 1-18, 20-23 and 26-28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 14 include the limitations: 'at least one .... where in the vaccine is capable of eliciting protective and/or immunoprophylactic antibodies against a pathogenic Neisseria strain'. Claims 2 and 3 include the limitations: 'protective and/or immunoprophylactic antibodies against ..... pathogenic Neisseria strain'. Claims 17 and 18 include the limitations: 'vaccine of claim ...., wherein said vaccine elicits protective and/or immunoprophylactic antibodies against at least ....% of pathogenic *Neisseria* strains'. Claims 6-8 include the recitation: 'the antibodies are elicited by ..... an immunogenic component of at least ...% of group B strains of *Neisseria meningitidis*'. Claim 15 includes the new limitations: 'vaccine of claim 1 further comprising a second immunogenic component, said second immunogenic component being an epitope on a *Neisseria* lipopolysaccharide inner core ..... wherein said phosphoethanolamine moiety of said second immunogenic component is linked to a different position of said HepII of the inner core than said phosphoethanolamine moiety of the immunogenic component of claim 1'. Claim 16 includes the limitations: 'vaccine of claim 1, wherein said immunogenic .....has two phosphoethanlamine moieties located at two positions on said HepII, a first said position being the 3-position, and a second said position being the 6- or the 7-position'. Claim 21, as amended, includes the limitation: 'vaccine of claim 1, wherein said immunogenic element' is capable of stimulating antibodies which are opsonic for pathogenic *Neisseria*'. Claims 22 and 23, as amended, include the limitation: 'a condition characterized by *Neisseria* ..... infection'. Claim 28, dependent from claim 27, now encompasses the vaccine of claim 1 wherein said *Neisseria* lipopolysaccharide inner core is of the commensal, *Neisseria*

lactamica, comprising at least one immunogenic lipopolysaccharide inner core component characterized by he presence of a phosphoethanolamine moetylinkd to a 3, 6, 7 or a combination thereof position of HepII of the inner core, wherein said vaccine is capable of eliciting protective and/or immunoprophylactic antibodies against a pathogenic *Neisseria* strain. However, there is no descriptive support for the limitations in the instant specification, as originally filed. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claims, or to point to specific pages and line numbers in the originally filed specification where support for the above-identified recitations can be found.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

54) Claims 1-18, 20-23 and 26-28 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The scope of the instant claims are indeterminate since the claims are very poorly written.

(a) Claim 2, 3, 17 and 18 are indefinite, confusing and/or improperly broadening in scope in the recitation 'immunoprophylactic antibodies against at least .....% of pathogenic *Neisseria* strains' [Emphasis added]. The claims depend from claim 1, which includes the recitation 'immunoprophylactic antibodies against **a** pathogenic *Neisseria* strain' [Emphasis added].

(b) Claim 9 is confusing in the use of the inconsistent limitations: 'said *Neisseria* LPS core'; 'this inner core'; and 'the inner core', because it is unclear whether or not the limitations are of same scope. It is suggested that Applicants use one consistent terminology.

(c) Analogous criticism applies to claim 10.

(d) Claim 20 is indefinite and confusing in the limitation 'lipopolysaccharide outer core of a bacterial capsule', because it is unclear how a bacterial capsule can comprise a 'lipopolysaccharide outer core'. It is known in the art that some bacterial lipopolysaccharides comprise an outer core and an inner core. But, what Applicants intend by the limitation 'a lipopolysaccharide outer core of a

bacterial capsule' is not understood. The metes and bounds of the claim are not clear.

(e) Claim 20 lacks proper antecedence and/or is improperly broadening in scope in the limitations: vaccine of claim 1, wherein said immunogenic component is 'an epitope accessible on a bacterium in the presence of a lipopolysaccharide outer core of a bacterial capsule'. Claim 20 depends from claim 1, wherein the immunogenic component, i.e., epitope, is limited to the one present on the 'lipopolysaccharide inner core' of a specific bacterium '*Neisseria*'. The dependent claim 20 however is improperly broadening in scope in the recitation of the broad and generic 'a bacterium'. The term 'a bacterium' is much broader in scope than the term 'a *Neisseria*'.

(f) Claim 1 is confusing in the limitation: 'to a 3, 6, 7, or a combination thereof, position of HepII of the inner core'. For the purpose of distinctly claiming the subject matter and for clarity, it is suggested that Applicants replace the limitation with --to position 3, 6, 7 or a combination thereof of HepII of the lipopolysaccharide inner core--.

(g) Analogous criticism applies to claim 15.

(h) Claim 6 is indefinite, confusing and improperly broadening in scope in the recitation: 'the antibodies are elicited by ..... an immunogenic component of at least 50% of group B strains of *Neisseria meningitidis*'. Claim 6 depends directly from claim 5 and indirectly from claim 1. The antibodies recited in claim 1 are required to be elicited by the vaccine that comprises 'at least one immunogenic component, said immunogenic component being an epitope on a *Neisseria*....'. From the poor claim language, it is unclear whether or not 'an immunogenic component of at least 50% of group B strains of *Neisseria meningitidis*' as recited in claim 6 is the same as or different from the immunogenic component recited in claim 1.

(i) Analogous criticism applies to claims 7 and 8.

(j) Claim 9 is vague and indefinite in the use of the abbreviated recitation: 'LPS', because it is unclear what does it stand for. It is suggested that Applicants use the full terminology at first occurrence with the abbreviation retained within the parentheses, in claim 9 or in the base claim 1.

(k) Claims 1-3, 11, 16 and 20 lack sufficient antecedent basis in the limitation: 'said immunogenic component', because the first recitation in line 2 of the amended claim 1 is 'at least one immunogenic component', but not 'an immunogenic component'.

(l) Analogous criticism applies to claim 14.

(m) Claims 4, 9, 10 and 12 lack sufficient antecedent basis in the limitation: 'the immunogenic component', because the first recitation in line 2 of the amended claim 1 is 'at least one immunogenic component', but not 'an immunogenic component'.

(n) Claim 16 is incorrect in the recitation: 'componenet'.

(o) Claim 12 is vague and inconsistent in the recitations: 'the LPS inner core' and 'the inner core LPS'. Claim 12 depends from claim 1 which includes the recitation: 'lipopolysaccharide inner core'.

(p) Claim 21 is incorrect and/or has improper antecedent basis in the limitation: 'said immunogenic element'. Claim 12 depends from claim 1, which does not recite any 'immunogenic element'.

(q) Claims 1 and 21 are of confusing or inconsistent scope. Claim 1 is drawn to a vaccine 'for the treatment of a disease caused by a pathogenic *Neisseria*'. Claim 21 depends from claim 1 and includes the limitation: vaccine of claim 1 'for the treatment of a condition characterized by *Neisseria meningitidis* infection'. It is unclear how the latter limitation further limits the former limitation in the base claim.

(r) Claims 2, 3, 17 and 18 are vague and indefinite in the recitation: 'at least .... % of pathogenic Neisseria strains', because it is unclear whether the recited percentage represents pathogenic *Neisseria* strains tested within Applicants' laboratory, or 60% or 70% of pathogenic *Neisseria* strains occurring in nature, or in any one environment.

(s) Analogous criticism applies to claims 6-8.

(t) Claims 9-12 and 20 include the recitation 'an epitope'. Claims 9-12 depend from claim 1 which already recites 'an epitope'. It is unclear whether 'an epitope' in claims 9-12 is the same as or different from the epitope recited in claim 1.

(u) Claim 27 is confusing and/or improperly broadening in scope in the limitations: '*Neisseria* lipopolysaccharide inner core' and 'commensal *Neisseria* inner core'.

(v) Claim 26 is vague in the recitation: 'vaccine of claim 1, which is a conjugated vaccine'. Claim 1 has been amended, which uses the open claim language allowing the claimed vaccine to 'comprise' components other than at least one immunogenic component or an epitope. It is unclear what component comprised in the claimed vaccine is conjugated.

(w) Claim 16 is improperly broadening in scope in the recitation: 'located at two positions on said HepII'. Claim 16 depends from claim 1, wherein the position of HepII of the inner core is limited to 3, 6, 7 or a combination thereof. The recitation 'two positions on said HepII' is broader in scope and includes positions other than 3, 6, or 7.

(x) Claims 9 and 10 are vague and indefinite in the limitation: 'structural equivalent'. It is not clear how much of the *Neisseria* LPS inner core's original structure has to be retained such that the resulting product can be considered as a 'structural equivalent thereof'. The metes and bounds of the structure encompassed in the limitation 'structural equivalent' is indeterminate.

(y) Claim 15 is confusing in the limitations: 'vaccine of claim 1' (see line 1) and 'the immunogenic component of claim 1' (see last line).

(z) Claims 22 and 23 are vague in the limitation: 'a condition characterized by *Neisseria* ..... infection', because it is unclear what is encompassed in the limitation. Does this include a clinical condition, non-clinical condition, symptomatic or non-symptomatic condition, subclinical condition, colonization, carriage, or sequelae?

(aa) Claims 2-18, 20-23 and 26-28, which depend directly or indirectly from claim 1 or 14, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

55) Claims 1-18, 20-23, 26 and 27 are rejected under 35 U.S.C § 102(b) as being anticipated by Hoogerhout *et al.* (NL 9,101,359 - original and English translated document) as evidenced by Goldschneider *et al.* (*J. Exp. Med.* 129: 1307-1326, 1969).

The page numbers pointed to in this rejection refer to the page number(s) in the translated document.

Hoogerhout *et al.* disclosed a vaccine composition for targeting at least one immunotype of meningococci comprising a saccharide part containing at least one epitope derived from a Gram negative bacterial LPS inner core region or a fragment derived from the same, and a conjugate comprising the same, which imparted cross-reactive immunity against one, two or more immunotypes of meningococcus including L1, L2 and L3 (see page 2, lines 1-15; page 5, third full paragraph; page 7, third full paragraph; paragraph bridging pages 18 and 19; page 29; and claims). The composition contains the meningococcal LPS oligosaccharide core region, or a fragment of the

same and a conjugate thereof. The LPS oligosaccharide can be non-toxic containing no lipid A and no lacto-N-neotetraose (see last paragraph on page 5; and page 6). The at least one meningococcal LPS core epitope contains one or more PEA groups and is from immunotype L3 (see paragraph bridging pages 6 and 7; third paragraph on page 18; page 28; and claim 33). The saccharide part in the vaccine composition is cross-reactive with more than one immunotype and provides protection against more than one immunotype (see first paragraph on page 7; and paragraph bridging page 7 and 8). The structure of the LPS core region of meningococcal immunotypes L1, L2, L3, L5 and L6 is shown in Figure 2. Figure 3 depicts the structure of the largest L1, L2 and L3 molecules (see page 7, second full paragraph). The basic structure contains alpha (1->2) bound GlucNAc unit(s), monosaccharides, and PEA groups (see forth paragraph on page 7). The composition can contain at the same time one or more saccharide core epitopes of more than one immunotype which elicits immunity specific for one immunotype or more than one diverse immunotypes (see paragraph bridging pages 7 and 8; and second paragraph on page 8). The saccharide parts imparting cross-reactive specific immunity against various immunotypes can be advantageously incorporated into the saccharide part of a saccharide-peptide conjugate (see second paragraph on page 8). The chemical formulae depicted on pages 8, 9, 27, 28, 33 and 34 are of meningococcal inner core oligosaccharides comprising KDO, GlcNAc, HepI, HepII and one or more PEA linked to HepII at position 3 or 6/7 and a glucose. A preferred saccharide-peptide conjugate contains a B-cell activating PEA-containing part exhibiting cross-reaction with at least two immunotypes of Gram negative bacteria, such as, meningococcal immunotypes L2 and L3; or L1 and L3; or L1, L2 and L3; or various immunotypes (see page 10). The saccharide part can be a fragment of the inner core region of the meningococcal LPS immunotype 6 (see paragraph 22 on page 21). Hoogerhout *et al.* taught that meningococcal immunotypes L3 and L2 cause approximately from 70% to 30% of the group B meningococcal meningitis and therefore the saccharide peptide conjugate preferably contains at least the saccharide core parts of L3 and/or L2 immunotypes (see third full paragraph on page 8). The saccharide-peptide conjugate contains the saccharide and at least one T-helper cell activating part of meningococcal class I OMP and offers protection against meningococci (see paragraph bridging pages 10 and 11). Hoogerhout *et al.* taught not to use the PEA group for coupling the meningococcal LPS oligosaccharide to a carrier peptide, but to retain the PEA group in the

conjugate since the group forms a part of a number of immunotype-specific epitopes. Hoogerhout *et al.* further taught that it is preferrable to make a saccharide-peptide conjugate with L3 meningococcal oligosaccharide in which the PEA groups and the KDO ring structure of meningococcal oligosaccharides are modified as little as possible (see second full paragraph on page 18). The saccharide part containing a minimal inner core oligosaccharide that imparts cross-reactive immunity, with one or more PEA groups built in therein, can be synthesized to obtain improved immunizing activity (see paragraph bridging pages 18 and 19). Hoogerhout *et al.* further taught that it is preferable that PEA groups of the saccharide be protected before and after coupling with the peptide (see first paragraph on page 21; and claim 57). Hoogerhout *et al.* discuss the art-recognized fact that the PEA group is of great importance for the immunological properties of the meningococcal LPS core (see the sentence bridging pages 24 and 25). Although Hoogerhout *et al.* are silent about the reactivity of the prior art immunogenic component to the specific monoclonal antibody recited in claim 14, the prior art immunogenic component is viewed as the same as Applicants' immunogenic component. Since the prior art immunogenic component is viewed as structurally the same as the one recited in the instant claim(s), it is expected to be reactive with Applicants' specific antibody produced by the hybridoma deposited under accession number IDAC 260900-1, which was inaccessible to Hoogerhout *et al.* at that time. The property of reactivity with the specific antibody recited by Applicants is viewed as an inherent property inseparable from the immunogenic component of Hoogerhout *et al.* That *N. meningitidis* qualifies as a commensal is inherent from the teachings of Hoogerhout *et al.* in light of what is well known in the art. For instance, Goldschneider *et al.* teach that *N. meningitidis* exists in normal human nasopharynx (see page 1307 of Goldschneider *et al.*, 1969).

Claims 1-18, 20-23, 26 and 27 are anticipated by Hoogerhout *et al.*

Remarks

56) Claims 1-18, 20-23 and 26-28 stand rejected.

57) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS

from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

58) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

59) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

60) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER